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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,380	02/28/2002	Daniel G. Chain	20555/1203301-US3	3496

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EXAMINER
EMCH, GREGORY S

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
11/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/084,380	CHAIN, DANIEL G.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,19,20,25,55,56,72,75,77-80 and 83-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,19,20,25,55,56,72,75,77-80 and 83-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/4/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Gregory S. Emch, Art Unit 1649.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 August 2007 has been entered.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 04 April 2007 is enclosed in this action.

Response to Amendment

Claims 14, 20, 77 and 83 have been amended as requested in the amendment filed on 29 August 2007. Following the amendment, claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80 and 83-86 are pending in the instant application.

Claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80 and 83-86 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Declarations under 37 CFR 1.132

Priority

In the reply filed 29 August 2007, Applicant again asserts that the current claims are entitled to a priority date of April 9, 1997, based on priority claimed to prior application nos. 09/402,820, which is the national stage of PCT/US98/06900, filed April 9, 1998, and the provisional application no. 60/041,850, filed April 9, 1997. Applicant asserts that support for the amended claim limitation of treating Alzheimer's disease by contacting soluble amyloid β peptide in the cerebrospinal fluid of an Alzheimer's patient can be found in the above applications and that such disclosures satisfy the requirements of 35 U.S.C. 112, first paragraph. Applicants submit two declarations under 37 CFR 1.132 as alleged evidence supporting the priority claim.

The declarations under 37 CFR 1.132 (i.e., the Federoff and Rock declarations) filed on 29 August 2007 are insufficient to establish benefit to a priority date of April 9, 1997. Therefore, the declarations are also insufficient to overcome the rejection of claims 14, 19, 20, 25, 55, and 56 under 35 U.S.C. 102(b) as being anticipated by Bard et al. (2000), the rejection of claims 14, 19, 20, 25, 55, 56, 72, 75, 77, 80, 83, and 86 under 35 U.S.C. 102(e) as being anticipated by US Patent 6,787,637 to Schenk and the

rejection of claims 78, 79, 84, and 85 under 35 U.S.C. 103(a) as being obvious over Schenk ('637 patent) in view of Saido et al. (1996) and Harigaya et al. (2000) as set forth previously.

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) or under 35 U.S.C. 120 as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosures of the prior-filed applications are directed to methods of treating Alzheimer's Disease (AD) via gene therapy, comprising delivering a gene encoding an "antisenilin molecule" (i.e., "a recombinant antibody molecule end-specific for the N-terminus or the C-terminus of an Aβ peptide") to a patient. However, the instant invention is not drawn to gene therapy methods; the instant invention is drawn to methods of treating AD "comprising contacting in vivo soluble amyloid β peptide in the cerebrospinal fluid of said patient with an exogenous free-end specific antibody which is targeted to a free N-terminus of amyloid β peptide or a free C-terminus," which encompasses both gene therapy and direct delivery methods. Moreover, at the time the disclosed invention in the '850 provisional application was filed, gene therapy was (and continues to be) a highly unpredictable art with regard to therapeutic effects.

Accordingly, the disclosures of the prior-filed applications, Application Nos. 60/041,850 (filed 04/09/1997), PCT US98/06900 (filed 04/09/1998), and 09/402,820 (filed 10/12/1999), fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for the instant invention. Hence, the instant application is correctly designated as a CIP of application no. 09/402,820, and thus the amended instant claims, which consist of subject matter that has not been disclosed prior to the filing of the instant application, are given a priority date of **February 28, 2002** (the filing date of the instant application).

In the Rock declaration, at item 9, it is stated, "(i) The provisional application describes all of the features set forth in the claimed methods for inhibiting accumulation or neurotoxicity of Aβ by contacting soluble Aβ in the cerebrospinal fluid of a patient suffering from Alzheimer's Disease with a free-end specific antibody to Aβ (ii) No later than April 9, 1997, a person of ordinary skill upon reading the provisional application would have concluded that the inventor was in possession of methods for inhibiting accumulation or neurotoxicity of Aβ by contacting soluble Aβ in the cerebrospinal fluid of a patient suffering from Alzheimer's Disease with an antibody; and (iii) A person of ordinary skill would have concluded that the method for contacting soluble Aβ in the cerebrospinal fluid of a patient suffering from Alzheimer's Disease with an antibody was not limited to gene therapy, i.e., gene therapy was only one of a number of approaches that could be used to contact soluble Aβ in the cerebrospinal fluid of a patient suffering from Alzheimer's Disease an antibody.." The declaration also points to excerpts from the provisional application that allegedly provide support for the statements outlined

above. For example, item 10 of the declaration states that the provisional application describes free-end specific antibodies generally, which can be administered through any means. In addition, Item 13 of the declaration states, "Furthermore, the provisional application discloses treating Alzheimer's disease generally, without reference to gene therapy. Thus, the provisional application states among the objects of the invention are to 'overcome the deficiencies in the prior art by providing a novel method for preventing or inhibiting the progression of Alzheimer's disease' (page 10, lines 11-13), 'provide a method for preventing or inhibiting the progression of Alzheimer's Disease by also inhibiting the interaction of amyloid-β peptides mediating amyloid-β induced neurotoxicity and inhibiting the amyloid-β induced complement activation and cytokine release involved in the inflammatory process associated with Alzheimer's Disease' (page 10, line 22 - page 11, line 2), and 'provide a pharmaceutical composition for preventing or inhibiting the progression of Alzheimer's Disease (page 11, lines 12-14).'" Item 15 of the declaration states that the skilled artisan would know that the antibodies disclosed in the provisional application could be administered directly.

These statements are not found persuasive for the following reasons. The examiner agrees that the provisional application describes the claimed methods for inhibiting accumulation or neurotoxicity of Aβ by contacting soluble Aβ in the cerebrospinal fluid of a patient suffering from Alzheimer's Disease with a free-end specific antibody to Aβ. However, the provisional application only contemplates providing the free-end specific antibody through gene therapy methods and the skilled artisan would recognize this fact upon reading its disclosure. The examiner also agrees

that the skilled artisan would know that gene therapy was only one of a number of approaches for antibody treatment. However, again, the artisan would have concluded that the provisional application and the invention described therein were only directed to gene therapy. The examiner also agrees that the provisional application describes free-end specific antibodies in general; but it only contemplates delivery of the antibody through gene therapy methods. Regarding the statements outlined in item 13, when read in context, the statements are also only directed to gene therapy methods and compositions. Moreover, regarding item 15, that the skilled artisan knows that antibodies could be delivered through another means does not relieve Applicants' burden of complying with the requirements of 35 U.S.C. 112, first paragraph.

In the Federoff declaration, at item 10, it is stated, "the information disclosed in the '850 application and the techniques that were then well known to those working in the field of gene therapy would have been sufficient to enable a person of ordinary skill in the field of gene therapy to use gene therapy to practice the methods called for in the claims of the subject patent application, for inhibiting accumulation or neurotoxicity of Aβ by contacting soluble Aβ in the CSF of a patient suffering from Alzheimer's Disease with a free-end specific antibody to Aβ." At Item 11, it is stated that the level of skill in the art of gene therapy for the nervous system was extremely high. At item 12, it is stated, "the '850 application would have been enabling for gene therapy at the time the application was filed" and "that the level of understanding of Alzheimer's disease, the level of skill in the art of gene therapy for neurological diseases, and the amount of guidance in the '850 application provide a rational, predictable basis for using the methods for treating

Alzheimer's called for in the claims pending in this application. In particular, a successful gene therapy protocol can be predicted by satisfying the following four criteria: i. An understanding of the disease mechanism; ii. Selection of a therapeutic gene with action on a target component that is necessary for the pathogenesis of the disease; iii. Selection of an appropriate virus vector that can deliver the therapeutic gene to the required anatomical area and express levels of the therapeutic gene sufficient to act on the target for the duration of disease; and iv. A means to deliver the therapeutic gene to the patient." In item 13, it is stated that the provisional application does satisfy the criteria mentioned in item 12. At item 14, it is stated that "the '850 application is enabling for gene therapy to treat Alzheimer's disease" because "the '850 application provides an abundance of guidance for production of an end-specific antibody to Aβ for use in a treatment for Alzheimer's disease." At item 21, it is stated, "I do not agree with the Examiner's conclusion that gene therapy was and continues to be a highly unpredictable art with regard to therapeutic effects. At the outset, I note that the Examiner provided no support for such a conclusion in connection with gene therapy treatment in general, and no support for such a conclusion in connection with gene therapeutic treatment of Alzheimer's disease, in particular."

These statements are not found persuasive for the following reasons. The examiner agrees that the level of skill in the art is high and that gene therapy methods were practiced at the time of filing. However, as stated previously, at the time the disclosed invention in the '850 provisional application was filed, gene therapy was (and continues to be) a highly unpredictable art with regard to therapeutic effects. Relevant

art from the time of filing, Verma et al. (Nature. 1997 Sep 18;389(6648):239-42) teaches that "although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (p.239, second paragraph). The Verma et al. reference also teaches, "the problem has been an inability to deliver genes efficiently and to obtain sustained expression," and that viral vectors are hampered by host responses (p.239, paragraphs 5-6). Regarding the potential for gene therapy to treat neurodegenerative disease as instantly claimed, the Verma et al. document teaches that retroviral vectors are not able to infect non-dividing cells such as those that make up the brain (p.240, paragraph 3). Although the Herpes simplex virus infects cells of the nervous system, and thus could be used in gene therapy, its use is hampered by cell toxicity and immunity to the virus from prior exposure (Verma et al. 241, final paragraph). The Verma et al. reference also raises concerns about the applicability of animal models to human treatment (p.240, paragraph 5). More recent art teaches that gene therapy treatment methods continue to lack therapeutic benefit. For example, Philips (J Pharm Pharmacol. 2001 Sep;53(9):1169-74) teaches that "although some evidence of gene transfer has been seen it has generally been inadequate for a meaningful clinical response. The major challenges have been delivery of DNA to the target cells and duration of expression" (abstract). As evidenced by the art, gene therapy methods for treatment of Alzheimer's disease, or any disease for that matter were highly unpredictable as it was at the time of filing.

Accordingly, the disclosures of the prior-filed applications, Application Nos. 60/041,850 (filed 04/09/1997), PCT US98/06900 (filed 04/09/1998), and 09/402,820 (filed 10/12/1999), fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for the instant invention. Hence, the instant application is correctly designated as a CIP of application no. 09/402,820, and thus the amended instant claims, which consist of subject matter that has not been disclosed prior to the filing of the instant application, are given a priority date of **February 28, 2002** (the filing date of the instant application).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80, and 83-86 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is maintained for reasons of record and as set forth below. The omitted steps are: the step of delivery of a free-end specific anti-Aβ antibody to a patient.

In the reply filed 29 August 2007, Applicant asserts, "a rejection under section 112, first paragraph would be improper, because the specification does not disclose administration to be an essential step." Applicant also believes that the current claim amendments address the grounds of rejection and that the amended claims are not lacking an essential step.

Applicant's arguments have been fully considered and are not found persuasive. Regardless of whether the specification teaches that administration is an essential step, the claims are indefinite because without an administration step, it is unclear to the artisan how exogenous antibodies would be present *in vivo*. In other words, it is unclear how the antibody gets into the patient in order to evoke the claimed method. Additionally, because the delivery of the antibody is missing, the contacting step is indefinite and thus open to interpretation as to where the contacting step occurs. Therefore, the current amendments are still indefinite.

Furthermore, as stated previously, claims 14, 20, 77 and 83 recite the limitation "said subject" in line 6 of each claim. There is insufficient antecedent basis for this limitation in the claims because the claims recite the term "patient" prior to the appearance of the term "subject."

Claim Rejections - 35 USC § 102

The rejection of claims 14, 19, 20, 25, 55, and 56 under 35 U.S.C. 102(b) as being anticipated by Bard et al. (2000) is maintained for reasons of record and as set forth below. .

Applicant argues that Bard does not qualify as prior art because the pending claims are entitled to a priority date of April 9, 1997.

Applicant's argument has been fully considered and is not found persuasive. As set forth above, the instant claims are given the priority date of February 28, 2002. As such, Bard et al. (2000) still qualifies as 102(b) prior art.

The rejection of claims 14, 19, 20, 25, 55, 56, 72, 75, 77, 80, 83, and 86 under 35 U.S.C. 102(e) as being anticipated by US Patent 6,787,637 is maintained for reasons of record and as set forth below.

Applicant argues that Schenk does not qualify as prior art because the pending claims are entitled to a priority date of April 9, 1997.

Applicant's argument has been fully considered but it is not found persuasive. As set forth above, the instant claims are given the priority date of February 28, 2002. As such, Schenk still qualifies as 102(e) prior art.

Claim Rejections - 35 USC § 103

The rejection of claims 77-80 and 83-86 under 35 U.S.C. 103(a) as being obvious over Schenk ('637 patent) in view of Saido et al. (1996) and Harigaya et al. (2000) is maintained for reasons of record and as set forth below.

Applicant argues that neither Schenk nor Harigaya qualify as prior art because the pending claims are entitled to a priority date of April 9, 1997.

Applicant's argument has been fully considered and is not found persuasive. As set forth above, the instant claims are given the priority date of February 28, 2002. As such, Schenk and Harigaya still qualify as prior art references.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
13 November 2007

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646